Clinical trials of ximelagatran

TrialResults-center www.trialresultscenter.org

1 atrial fibrillation

Trial	Treatments	Patients	Trials design and methods
ximelagatran vs warfarin standard dose			
SPORTIF V , 2005 n=1960/1962 follow-up: 20 months	ximelegatran 36 mg twice daily versus warfarin standard dose(target INR 2-3)	One or more stroke risk factor in addition to atrial fibrillation.High risk patients with non valvular atrial fibrillation.	Parallel groups Double blind north america
SPORTIF II (ximelagatran vs warfarin standard dose) , 2002 n=187/67 follow-up: 16 weeks	ximelegatran 20,40,60 mg twice daily versus warfarin standard dose(target INR 2-3)	Medium to high risk patients with chronic non valvular atrial fibrillation.	Parallel groups Open Europe ,USA
SPORTIF III , 2003 n=1704/1703 follow-up: 17.4 months	ximelagatran 36 mg twice daily versus warfarin standard dose (target INR 2-3)	One or more stroke risk factor in addition to AF.High risk patients with non valvular atrial fibrillation.	Parallel groups Open europe,asia,australasia

More details and results :

- antithrombotics for atrial fibrillation in primary prevention of thromboembolic events at http://www.trialresultscenter.org/go-Q57
- direct antithrombins for atrial fibrillation in all type of patients at http://www.trialresultscenter.org/go-Q368
- direct oral anticoagulant (DAO) for atrial fibrillation in all type of patients at http://www.trialresultscenter.org/go-Q391

References

SPORTIF V, 2005:

Halperin JL Ximelagatran compared with warfarin for prevention of thromboembolism in patients with nonvalvular atrial fibrillation: Rationale, objectives, and design of a pair of clinical studies and baseline patient characteristics (SPORTIF III and V). Am Heart J 2003 Sep;146:431-8 [12947359]

Albers GW, Diener HC, Frison L, Grind M, Nevinson M, Partridge S, Halperin JL, Horrow J, Olsson SB, Petersen P, Vahanian A Ximelagatran vs warfarin for stroke prevention in patients with nonvalvular atrial fibrillation: a randomized trial. JAMA 2005 Feb 9;293:690-8 [15701910]

SPORTIF II (ximelagatran vs warfarin standard dose), 2002:

Petersen P, Grind M, Adler J Ximelagatran versus warfarin for stroke prevention in patients with nonvalvular atrial fibrillation. SPORTIF II: a dose-guiding, tolerability, and safety study. J Am Coll Cardiol 2003 May 7;41:1445-51 [12742279]

SPORTIF III, 2003:

Olsson SB Stroke prevention with the oral direct thrombin inhibitor ximelagatran compared with warfarin in patients with non-valvular atrial fibrillation (SPORTIF III): randomised controlled trial. Lancet 2003 Nov 22;362:1691-8 [14643116]

2 acute coronary syndrome

Trial	Treatments	Patients	Trials design and methods
ximelagatran vs placebo			
ESTEEM , 2003 n=1245/638 follow-up: 6 months	oral ximelagatran at doses of 24 mg, 36 mg, 48 mg, or 60 mg twice daily versus placebo	patients who had had recent ST-elevation or non-STelevation myocardial infarction	Parallel groups double-blind

More details and results :

- antithrombotics for acute coronary syndrome in all type of patients at http://www.trialresultscenter.org/go-Q24
- anticoagulant for acute coronary syndrome in All ACS (including AMI) at http://www.trialresultscenter.org/go-Q167
- direct factor Xa inhibitors for acute coronary syndrome in all type of patients at http://www.trialresultscenter.org/go-Q345
- antithrombotics for acute coronary syndrome in patients with a recent ACS at http://www.trialresultscenter.org/go-Q387
- direct oral anticoagulant (DAO) for acute coronary syndrome in all type of patients at http://www.trialresultscenter.org/go-Q480

References

ESTEEM, 2003:

Wallentin L, Wilcox RG, Weaver WD, Emanuelsson H, Goodvin A, Nystrm P, Bylock A Oral ximelagatran for secondary prophylaxis after myocardial infarction: the ESTEEM randomised controlled trial. Lancet 2003 Sep 6;362:789-97 [13678873]

3 thrombosis prevention

Trial	Treatments	Patients	Trials design and methods
ximelagatran vs Dalteparin			
METHRO I , 2002 n=103 follow-up: 69 days	Melagatran 14 mg s.c. immediately before surgery, melagatran at 20.00 hours, then ximelagatran 624 mg orally b.d. for 69 days versus Dalteparin 5000 IU o.d., started evening before surgery for 69 days	adults undergoing hip or knee replacement	parallel group open Swedish
METHRO II , 2002 n=1495/381 follow-up: 710 days	Melagatran 13 mg s.c. immediately before surgery,melagatran same day, then ximelagatran 824 mg orally b.d. for 710 days versus Dalteparin 5000 IU o.d., started evening before surgery for 710 days	undergoing hip or knee replacement	Parallel groups double-blind
ximelagatran vs Enoxaparin			
Platinum (Colwell) , 2003 n=906/910 follow-up: 712 days	Ximelagatran 24 mg orally b.d., starting at least 12 h after surgery for 712 days versus Enoxaparin 30 mg s.c. b.d.,starting at least 12 h after surgery for 712 days	adults undergoing hip replacement	parallel group double-blind USA, Canada, Israel, Mexico,Argentina, South Africa
METHRO III , 2002 n=2788 follow-up: 811 days	Melagatran 3 mg s.c. 412h after surgery, then ximelagatran24 mg orally b.d. for 710 days versus Enoxaparin 40 mg s.c. o.d. 12 h before surgery for 710 days	hip or knee replacement	double-blind Europe, South Africa
Phase II (Heit) , 2001 n=600 follow-up: 612 days	Ximelagatran 8, 12, 18 or 24 mgorally b.d., at least 12 h after surgery for 612 days versus Enoxaparin 30 mg s.c. b.d.,starting at least 12 h after surgery for 612 days	adults (age>18 years and weight at least 40 kg) undergoing knee replacements	parallel group double-blind North American
EXPRESS , 2003 n=2835 follow-up: 811 days	Melagatran 2 mg s.c. up to 30 min before surgery, then melagatran 3 mg at least 8 hafter surgery, then ximelagatran 24 mg orally b.d. for 811 days versus Enoxaparin 40 mg s.c. o.d.,starting 12 h before surgery for 811 days	hip or knee replacement	parallel group double-blind Europe

More details and results :

- antithrombotics for thrombosis prevention in orthopedic surgery at http://www.trialresultscenter.org/go-Q37
- antithrombotics for thrombosis prevention in elective major knee surgery at http://www.trialresultscenter.org/go-Q38
- antithrombotics for thrombosis prevention in elective hip replacement at http://www.trialresultscenter.org/go-Q39
- direct antithrombins for thrombosis prevention in orthopedic surgery at http://www.trialresultscenter.org/go-Q185

References

METHRO I, 2002:

Eriksson BI, Arfwidsson AC, Frison L, Eriksson UG, Bylock A, Klebo P, Fager G, Gustafsson D A dose-ranging study of the oral direct thrombin inhibitor, ximelagatran, and its subcutaneous form, melagatran, compared with dalteparin in the prophylaxis of thromboembolism after hip or knee replacement: METHRO I. MElagatran for THRombin inhibition in Orthopaedic surgery. Thromb Haemost 2002;87:231-7 [11858482]

METHRO II, 2002:

Eriksson BI, Bergqvist D, Klebo P, Dahl OE, Lindbratt S, Bylock A, Frison L, Eriksson UG, Welin L, Gustafsson D Ximelagatran and melagatran compared with dalteparin for prevention of venous thromboembolism after total hip or knee replacement: the METHRO II randomised trial. Lancet 2002;360:1441-7 [12433510]

Platinum (Colwell), 2003:

Colwell CW Jr, Berkowitz SD, Davidson BL, Lotke PA, Ginsberg JS, Lieberman JR, Neubauer J, McElhattan JL, Peters GR, Francis CW Comparison of ximelagatran, an oral direct thrombin inhibitor, with enoxaparin for the prevention of venous thromboembolism following total hip replacement. A randomized, double-blind study. J Thromb Haemost 2003;1:2119-30 [14521593]

METHRO III, 2002:

Eriksson BI, Agnelli G, Cohen AT, Dahl OE, Mouret P, Rosencher N, Eskilson C, Nylander I, Frison L, Ogren M Direct thrombin inhibitor melagatran followed by oral ximelagatran in comparison with enoxaparin for prevention of venous thromboembolism after total hip or knee replacement. Thromb Haemost 2003;89:288-96 [12574809]

Mouret P [The oral direct thrombin inhibitor Ximelagatran Prophylaxis of venous thromboembolism in hip and knee replacement] Hamostaseologie 2002;22:21-4 [12215757]

Eriksson BI Clinical experience of melagatran/ximelagatran in major orthopaedic surgery. Thromb Res 2003;109 Suppl 1:S23-9 [12818631]

Phase II (Heit), 2001:

Heit JA, Colwell CW, Francis CW, Ginsberg JS, Berkowitz SD, Whipple J, Peters G Comparison of the oral direct thrombin inhibitor ximelagatran with enoxaparin as prophylaxis against venous thromboembolism after total knee replacement: a phase 2 dose-finding study. Arch Intern Med 2001;161:2215-21 [11575978]

EXPRESS, 2003:

Eriksson BI, Agnelli G, Cohen AT, Dahl OE, Lassen MR, Mouret P, Rosencher N, Klebo P, Panfilov S, Eskilson C, Andersson M, Freij A The direct thrombin inhibitor melagatran followed by oral ximelagatran compared with enoxaparin for the prevention of venous thromboembolism after total hip or knee replacement: the EXPRESS study. J Thromb Haemost 2003;1:2490-6 [14675083]

Glynn O The express study: preliminary results. Int J Clin Pract 2003;57:57-9 [12587945]

4 venous thrombosis

Trial	Treatments	Patients	Trials design and methods
ximelagatran vs discontinuation			
THRIVE III , 2003 n=612/611 follow-up: 18 months	ximelagatran 24 mg twice daily for 18 months versus placebo for 18 months	patients with venous thromboembolism who had undergone six months of anticoagulant therapy	Parallel groups double blind 18 countries
ximelagatran vs placebo			
Schulman (subgroup) , 2003 n=NA follow-up: 18 months	extended treatment with Ximelagatran 24mg twice daily after initial anticoagulant treatment for 6 months versus placebo (initial anticoagulant treatment for 6 months)	study subgroup of patients with active cancer in the previous 5 years treated for DVT or pulmonary embolism for 6 months without recurrence	Parallel groups single blind and outcome ass.
THRIVE 3 , 2003 n=612/611 follow-up:	ximelagatran (24 mg) versus placebo	patients with venous thromboembolism who had undergone six months of anticoagulant therapy	
ximelagatran vs LMWH/VKA			
Fiessinger , 2005 n=NA follow-up:	ximelagatran 36 mg twice daily versus subcutaneous enoxaparin, 1 mg/kg twice daily, for 5 to 20 days followed by warfarin adjusted to maintain an international normalized ratio of 2.0 to 3.0.	patients with acute deep vein thrombosis	double blind
ximelagatran (without LMWH) vs LMWH/VKA			
THRIVE I , 2003 n=NA follow-up:	oral ximelagatran (24, 36, 48 or 60 mg twice daily) for 2 weeks versus dalteparin and warfarin for 2 weeks	Patients with acute DVT	

More details and results :

- antithrombotics for venous thrombosis in all type of patients at http://www.trialresultscenter.org/go-Q101
- antithrombotics for venous thrombosis in patients with cancer at http://www.trialresultscenter.org/go-Q103
- antithrombotics for venous thrombosis in secondary prevention of VTE at http://www.trialresultscenter.org/go-Q149
- direct factor Xa inhibitors for venous thrombosis in all type of patients at http://www.trialresultscenter.org/go-Q372

- direct oral anticoagulant (DAO) for venous thrombosis in all types of patients at http://www.trialresultscenter.org/go-Q505
- antithrombotics for venous thrombosis in secondary prevention - 2 at http://www.trialresultscenter.org/go-Q682

References

THRIVE III, 2003:

Schulman S, Whlander K, Lundstrm T, Clason SB, Eriksson H Secondary prevention of venous thromboembolism with the oral direct thrombin inhibitor ximelagatran. N Engl J Med 2003 Oct 30;349:1713-21 [14585939]

Schulman S, Lundstrm T, Wlander K, Billing Clason S, Eriksson H Ximelagatran for the secondary prevention of venous thromboembolism: a complementary follow-up analysis of the THRIVE III study. Thromb Haemost 2005 Oct;94:820-4 [16270637]

Schulman (subgroup), 2003:

Schulman S, Whlander K, Lundstrm T, Clason SB, Eriksson H Secondary prevention of venous thromboembolism with the oral direct thrombin inhibitor ximelagatran. N Engl J Med 2003;349:1713-21 [14585939]

THRIVE 3, 2003:

Schulman S, Whlander K, Lundstrm T, Clason SB, Eriksson H Secondary prevention of venous thromboembolism with the oral direct thrombin inhibitor ximelagatran. N Engl J Med 2003;349:1713-21 [14585939] 10.1056/NEJMoa030104

Fiessinger , 2005:

Fiessinger JN, Huisman MV, Davidson BL, Bounameaux H, Francis CW, Eriksson H, Lundstrm T, Berkowitz SD, Nystrm P, Thorsn M, Ginsberg JS Ximelagatran vs low-molecular-weight heparin and warfarin for the treatment of deep vein thrombosis: a randomized trial. JAMA 2005 Feb 9;293:681-9 [15701909]

THRIVE I, 2003:

Eriksson H, Whlander K, Gustafsson D, Welin LT, Frison L, Schulman S A randomized, controlled, dose-guiding study of the oral direct thrombin inhibitor ximelagatran compared with standard therapy for the treatment of acute deep vein thrombosis: THRIVE I. J Thromb Haemost 2003 Jan;1:41-7 [12871538]

Entry terms: ximelagatran, xi-melagatran, Exanta, H 376 95, H 376-95,